

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing:

10 September 1999 (10.09.99)

International application No.:

PCT/AU99/00136

Applicant's or agent's file reference:

91570

International filing date:

05 March 1999 (05.03.99)

Priority date:

06 March 1998 (06.03.98)

Applicant:

COIA, Gregory et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International preliminary Examining Authority on:

09 July 1999 (09.07.99)



in a notice effecting later election filed with the International Bureau on:

2. The election



was



was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer:

J. Zahra

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 91570	<div style="display: flex; justify-content: space-between;"> <div style="text-align: center;">FOR FURTHER ACTION</div> <div>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</div> </div>	
International application No. PCT/AU 99/00136	International filing date (day/month/year) 5 March 1999	(Earliest) Priority Date (day/month/year) 6 March 1998

Applicant
DIATECH PTY LTD

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of ~~3~~ ⁴ sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (See Box II).

4. With regard to the title, ☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract, ☒ the text is approved as submitted by the applicant

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ None of the figures

☐ because the applicant failed to suggest a figure

☐ because this figure better characterizes the invention

☐

A. CLASSIFICATION OF SUBJECT MATTER		
Int Cl ⁶ : C12N 15/12, 15/13; C07K 14/705, 14/73, 14/665, 14/745 A61K 38/31, 38/04; 39/395 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) As above		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched As below		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) <u>Medline & CA</u> : Receptors, antigen: CTLA.4, CD28, ICOS, <u>WPAT</u> :- variable region or domain, CDR, variable and region or domain, CDR, soluble/solubility, CTLA-4, CD28, ICOS		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Jung S and Pluckthun A. Protein Eng. 1997. 10(8): 959-966	1-10, 13
Y	Patten et al. J Immunol. 1993. 150(6): 2281-2294	All
Y	WO 91/10438 (Protein Design Labs Inc) 1991	All
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family	
Date of the actual completion of the international search 30 March 1999		Date of mailing of the international search report 13 APR 1999
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No.: (02) 6285 3929		Authorized officer GILLIAN ALLEN Telephone No.: (02) 6283 2266

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Peach RJ et al. J Exp Med. 1994. 180(6): 2049-2058	All
Y	Davies J and Reichman L. Protein Eng. 1996. 9(6): 531-537. Medline Abstract. Cited by applicant	16-17

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU 99/00136

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member	
WO	9110438	AU	71825/91
		US	5216132
END OF ANNEX			

PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 91570	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International application No. PCT/AU 99/00136	International filing date (<i>day/month/year</i>) 5 March 1999	Priority Date (<i>day/month/year</i>) 6 March 1998
International Patent Classification (IPC) or national classification and IPC Int. Cl. ⁶ C12N 15/12, 15/13; C07K 14/705, 14/73, 14/665, 14/745; A61K 38/04, 38/31, 39/395		
Applicant Diatech Pty Ltd		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.																								
2.	This REPORT consists of a total of 4 sheets, including this cover sheet. <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of sheet(s).																								
3.	This report contains indications relating to the following items: <table style="width: 100%; margin-top: 10px;"> <tr> <td style="width: 5%;">I</td> <td style="width: 5%; text-align: center;"><input checked="" type="checkbox"/></td> <td>Basis of the report</td> </tr> <tr> <td>II</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Priority</td> </tr> <tr> <td>III</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td>IV</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Lack of unity of invention</td> </tr> <tr> <td>V</td> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td>VI</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Certain documents cited</td> </tr> <tr> <td>VII</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Certain defects in the international application</td> </tr> <tr> <td>VIII</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Certain observations on the international application</td> </tr> </table>	I	<input checked="" type="checkbox"/>	Basis of the report	II	<input type="checkbox"/>	Priority	III	<input type="checkbox"/>	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	IV	<input type="checkbox"/>	Lack of unity of invention	V	<input checked="" type="checkbox"/>	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	VI	<input type="checkbox"/>	Certain documents cited	VII	<input type="checkbox"/>	Certain defects in the international application	VIII	<input type="checkbox"/>	Certain observations on the international application
I	<input checked="" type="checkbox"/>	Basis of the report																							
II	<input type="checkbox"/>	Priority																							
III	<input type="checkbox"/>	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability																							
IV	<input type="checkbox"/>	Lack of unity of invention																							
V	<input checked="" type="checkbox"/>	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement																							
VI	<input type="checkbox"/>	Certain documents cited																							
VII	<input type="checkbox"/>	Certain defects in the international application																							
VIII	<input type="checkbox"/>	Certain observations on the international application																							

Date of submission of the demand 15 July 1999	Date of completion of the report 15/10/99
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No. (02) 6285 3929	Authorized Officer Gillian Allen Telephone No. (02) 6283 2266

L Basis of the report

1. With regard to the elements of the international application:*
- ☒ the international application as originally filed.
- ☐ the description, pages , as originally filed,
 pages , filed with the demand,
 pages , filed with the letter of .
- ☐ the claims, pages , as originally filed,
 pages , as amended (together with any statement) under Article 19,
 pages , filed with the demand,
 pages , filed with the letter of .
- ☐ the drawings, pages , as originally filed,
 pages , filed with the demand,
 pages , filed with the letter of .
- ☐ the sequence listing part of the description:
 pages , as originally filed
 pages , filed with the demand
 pages , filed with the letter of .
2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:
- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).
3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, was on the basis of the sequence listing:
- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished
4. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/fig.
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims 1-33	YES
	Claims	NO
Inventive step (IS)	Claims 1-33	YES
	Claims	NO
Industrial applicability (IA)	Claims 1-28, 30-33	YES
	Claims	NO

2. Citations and explanations (Rule 70.7)Citations

- D1. Jung S and Pluckthorn A. Protein Eng. 1997. 10(8): 959-966.
D2. Patten et al. J Immunol. 1993. 150(6): 2281-2294
D3. WO 91/10438. (Protein Design Labs Inc.) 1991
D4. Peach et al. J Exp Med. 1994. 180(6): 2049-2058.
D5. Davies and Reichman. Protein Eng. 1996. 9(6): 531-537.

Novelty.

There is no disclosure in the prior art that replacement or modification of the CDR loops of antibody like molecules results in molecules with improved solubility. It is accepted that the specific modifications of claim 3 have been shown to be associated with increased solubility of the V-like domains. Therefore, all claims are novel.

Inventive Step.

It is admitted by the applicant that the V-like domains of the non-antibody ligands of the present invention bear a strong resemblance to the variable domains of both immunoglobulin antibodies and the T cell receptor. Therefore it is considered that one skilled in the art would consider techniques and changes that have been applied to Ig and/or TCR molecules as being well worth consideration as at least a starting point in the manipulation of the non-antibody ligands of the present application.

D1 teaches that it is possible to improve the solubility of improperly folded antibody Fv molecules, whilst retaining its specificity, by grafting the CDR loops to a humanised antibody framework. However, this does not directly bear on the solution found by the present applicant, which grafts foreign CDR loops onto the V-like domain of non-antibody molecules, changing the specificity and improving the solubility.

D2 discloses the transfer of CDR loops between different T cell receptors. This discloses change in specificity, but there is no disclosure that altered solubility was sought or observed.

D3 discloses that the CDR loops of CD28 and CTLA-4 determine the binding specificities of these molecules, and that alteration to these CDR loops changes binding specificity. However, there is no suggestion that grafting or changing the CDR loops has any effect on solubility.

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of : Box V

D2 and D3 provide guidance on construction of alternate forms of V-like domains. However, since neither addresses the problem of solubility, they are not considered to anticipate forms of the V-like domain which have improved solubility because they have modified or grafted CDR loops.

D4 discloses soluble T cell receptor peptides obtained by fusing the V β variable domain, which comprises the CDR loops to a constant region of any immunoglobulin superfamily molecule, which would include the non-antibody ligands of the present invention. However, although this addresses the solubility problem, the citation does not teach or suggest direct modification of CDR loops

D5 discloses camelisation of the V_H region, with the modification of the V_H region providing an intradomain disulphide bond which improves folding stability. One skilled in the art would tend to associate improved folding stability with improved solubility. However, this citation is not specifically directed to improvements in solubility, nor to non-antibody ligands.

Therefore all claims are considered inventive over the prior art.

Industrial Applicability.

Claim 29 is to method of treatment of the human body. No unified criterion exists within the member countries of the PCT as to the industrial applicability of such claims. The remaining claims are industrially applicable.

PCT REQUEST

91570

Original (for SUBMISSION) - printed on 05.03.1999 11:30:16 AM

0	For receiving Office use only	
0-1	International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	
0-4	Form - PCT/RO/101 PCT Request	
0-4-1	Prepared using	PCT-EASY Version 2.80 (updated 01.01.1999)
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	Receiving Office (specified by the applicant)	Australian Patent Office (RO/AU)
0-7	Applicant's or agent's file reference	91570
I	Title of invention	V-LIKE DOMAIN BINDING MOLECULES
II	Applicant	
II-1	This person is:	applicant only
II-2	Applicant for	all designated States
II-4	Name	DIATECH PTY LTD
II-5	Address:	GPO Box 2434 Brisbane, Queensland 4001 Australia
II-6	State of nationality	AU
II-7	State of residence	AU
II-8	Telephone No.	-
II-9	Facsimile No.	-
II-10	e-mail	-
III-1	Applicant and/or inventor	
III-1-1	This person is:	applicant and inventor
III-1-2	Applicant for	US only
III-1-4	Name (LAST, First)	COIA, Gregory
III-1-5	Address:	73 Union Street Brunswick, Victoria 3056 Australia
III-1-6	State of nationality	AU
III-1-7	State of residence	AU

PCT REQUEST

91570

Original (for SUBMISSION) - printed on 05.03.1999 11:30:16 AM

III-2	Applicant and/or inventor	
III-2-1	This person is:	applicant and inventor
III-2-2	Applicant for	US only
III-2-4	Name (LAST, First)	GALANIS, Maria
III-2-5	Address:	5 Rowitta Drive Glen Waverley, Victoria 3150 Australia
III-2-6	State of nationality	AU
III-2-7	State of residence	AU
III-3	Applicant and/or inventor	
III-3-1	This person is:	applicant and inventor
III-3-2	Applicant for	US only
III-3-4	Name (LAST, First)	HUDSON, Peter John
III-3-5	Address:	36 Fuschia Street Blackburn, Victoria 3130 Australia
III-3-6	State of nationality	AU
III-3-7	State of residence	AU
III-4	Applicant and/or inventor	
III-4-1	This person is:	applicant and inventor
III-4-2	Applicant for	US only
III-4-4	Name (LAST, First)	IRVING, Robert Alexander
III-4-5	Address:	11 Honeysuckle Avenue Mulgrave, Victoria 3170 Australia
III-4-6	State of nationality	AU
III-4-7	State of residence	AU
III-5	Applicant and/or inventor	
III-5-1	This person is:	applicant and inventor
III-5-2	Applicant for	US only
III-5-4	Name (LAST, First)	NUTTALL, Stewart Douglas
III-5-5	Address:	75 Ford Street Ivanhoe, Victoria 3079 Australia
III-5-6	State of nationality	AU
III-5-7	State of residence	AU

PCT REQUEST

91570

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IV-1	Agent or common representative; or address for correspondence The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent
IV-1-1	Name	F B RICE & CO
IV-1-2	Address:	605 Darling Street Balmain, New South Wales 2041 Australia
IV-1-3	Telephone No.	(612) 9810 7133
IV-1-4	Facsimile No.	(612) 9810 8200
IV-1-5	e-mail	partners@fbrice.com.au
V	Designation of States	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW SD SZ UG ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE CH&LI CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AL AM AT AU AZ BA BB BG BR BY CA CH&LI CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

PCT REQUEST

91570

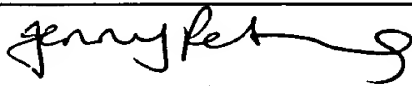
Original (for SUBMISSION) - printed on 05.03.1999 11:30:16 AM

V-5	Precautionary Designation Statement In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	Exclusion(s) from precautionary designations	NONE
VI-1	Priority claim of earlier national application	
VI-1-1	Filing date	06 March 1998 (06.03.1998)
VI-1-2	Number	PP2210
VI-1-3	Country	AU
VI-2	Priority document request The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):	VI-1

PCT REQUEST

91570

Original (for SUBMISSION) - printed on 05.03.1999 11:30:16 AM

VII-1	International Searching Authority Chosen	Australian Patent Office (ISA/AU)	
VIII	Check list	number of sheets	electronic file(s) attached
VIII-1	Request	6	-
VIII-2	Description	91	-
VIII-3	Claims	4	-
VIII-4	Abstract	1	91570abs.txt
VIII-5	Drawings	15	-
VIII-7	TOTAL	117	
	Accompanying items	paper document(s) attached	electronic file(s) attached
VIII-8	Fee calculation sheet	✓	-
VIII-16	PCT-EASY diskette	-	diskette
VIII-18	Figure of the drawings which should accompany the abstract		
VIII-19	Language of filing of the international application	English	
IX-1	Signature of applicant or agent		
IX-1-1	Name	F B RICE & CO	
IX-1-2	Name of signatory	Jenny Petering	

FOR RECEIVING OFFICE USE ONLY

10-1	Date of actual receipt of the purported international application	
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PCT REQUEST

91570

Original (for SUBMISSION) - printed on 05.03.1999 11:30:16 AM

10-2	Drawings:	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/AU
10-6	Transmittal of search copy delayed until search fee is paid	

FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	
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PCT (ANNEX - FEE CALCULATION SHEET)

91570

Original (for **SUBMISSION**) - printed on 05.03.1999 11:30:16 AM

(This sheet is not part of and does not count as a sheet of the international application)

0	For receiving Office use only		
0-1	International Application No.		
0-2	Date stamp of the receiving Office		
0-4	Form - PCT/RO/101 (Annex)		
0-4-1	PCT Fee Calculation Sheet Prepared using	PCT-EASY Version 2.80 (updated 01.01.1999)	
0-9	Applicant's or agent's file reference	91570	
2	Applicant	DIATECH PTY LTD, et al.	
12	Calculation of prescribed fees	fee amount/multiplier	total amounts (AUD)
12-1	Transmittal fee T	⇒	100
12-2	Search fee S	⇒	800
12-3	International fee Basic fee (first 30 sheets) b1	722	
12-4	Remaining sheets	87	
12-5	Additional amount (X)	17	
12-6	Total additional amount b2	1,479	
12-7	b1 + b2 = B	2,201	
12-8	Designation fees Number of designations contained in international application	77	
12-9	Number of designation fees payable (maximum 10)	10	
12-10	Amount of designation fee (X)	166	
12-11	Total designation fees D	1,660	
12-12	PCT-EASY fee reduction R	-222	
12-13	Total International fee (B+D-R) I	⇒	3,639
12-14	Fee for priority document Number of priority documents requested	1	
12-15	Fee per document (X)	30	
12-16	Total priority document fee P	⇒	30
12-17	TOTAL FEES PAYABLE (T+S+I+P)	⇒	4,569
12-19	Mode of payment	cheque	

VALIDATION LOG AND REMARKS

13-1-1	Applicant remarks Annotate	Sequence Listing pages have been included as part of the description for the fee calculation sheet.
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